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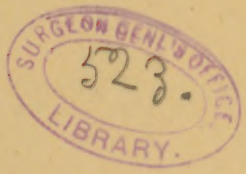

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LEUKEMIA IN INFANTS.

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LITTLE is known concerning the etiology of this disease. Several cases are on record which prove that a pregnant woman with leukemia cannot directly transmit it to her offspring. Cameron [1] reports a case where the child of a leukemic mother died on the fourth day, and the autopsy failed to reveal any evidences of leukemia. Greene,[2] also, reports a case in which a leukemic mother was delivered of a healthy child. Sänger [3] had a case where a leukemic mother gave birth to a healthy child which did not develop leukemia, although kept under observation for some time, while in Degle's [4] case the child was feeble but showed no signs of leukemia. Askanazy [5] also reports a case where a woman with myelogenous leukemia was delivered at full term of a slightly macerated fetus, which, on autopsy, showed no evidence of leukemia. On the other hand, Sänger [3] reports a case in which a healthy woman was delivered of a dead-born fetus at the thirty-second week, which, on autopsy, showed well-marked signs of leukemia. It is possible, however, that the tendency to the disease may be transmitted. Several cases are on record of its occurrence in more than one member of the same family. Griffith [6] quotes cases of Casati [7] and Eichhorst [8] bearing on this point; while Osler [9] relates a very interesting case of Cameron's in which the dis-

ease was present in three generations. Biermer [10] reports its occurrence in sisters, but it is hardly possible to rule out rhachitis in this instance. Senator's [11] cases in twins are also open to the suspicion of anemia infantum pseudoleukemica. Ortner,[12] also, saw the disease in sisters.

Rhachitis is supposed to have some etiological connection with the disease in children, but its influence is probably not as great as has been supposed. It must be remembered in this connection that very few of the so-called cases of leukemia in children have been carefully worked up and reported. In very few has a blood count been made, and in only one or two has there been a differential count of the white corpuscles. Fox and Ball [13] in several hundred cases of rhachitis found the spleen enlarged in twenty-five per cent. In sixty-three cases of splenic tumor in infants, which they examined, rhachitis could not be positively excluded in one, and in almost all was very marked. In the few cases in which an examination of the blood was made nothing more than a slight leucocytosis was ever found. Carr [14] obtained the same results in a few cases which he examined. Kultner,[15] also, speaks of the frequency of splenic tumor in rhachitis and calls attention to the ease with which splenic enlargement takes place in children. He examined the blood in ten cases, and in none of them found any evidence of leukemia. This frequent association of splenic tumor with rhachitis is undoubtedly the source of the common acceptation of rhachitis as a cause of leukemia. It must be said, however, that rhachitis has been present in nearly all of the more carefully reported cases of leukemia in children. Its true relation, however, can only be determined by the examination of the blood by modern methods in a large number of cases.

The same doubt hangs about the relation of syphilis

to leukemia in children. Fox and Ball[13] found the spleen enlarged in forty-eight per cent. of their cases of inherited syphilis, and in sixty-three cases of splenic tumor in infants, forty-one had inherited syphilis. The examination of the blood in these cases also showed at most a slight leucocytosis.

Leukemia has sometimes developed in adults after trauma. Mosler[16] has reported a rather doubtful case of this sort in a child.

The disease is most common in middle-life. Birch-Hirschfeld,[17] in 1878, out of 201 cases collected by him, found only four under one year. Hayem,[18] in 1879, expressed the opinion that only four or five cases had been seen in children under one year. Baginsky,[19] on the other hand, thinks that from fifteen to twenty per cent. of the cases are seen in children under ten years, and Gerhardt[20] thinks it is as frequent in children as it is later in life. But little reliance can be placed on these figures, however, because of the possibilities of errors in diagnosis.

Males are generally more prone to the disease than females. This rule seems to hold good, also, as regards children, so far as the figures are of use in so small a number of cases.

I have been able to collect 20 cases of leukemia in infants out of literature. The diagnosis in the majority, however, must be regarded as doubtful. In the earlier cases no examination of the blood was made, and in some of these the diagnosis rests entirely on the clinical picture, no autopsy having been made. In many of the later cases a blood count was made, but in very few has the character of the white corpuscles been noted, and in only one has a differential count of them been made. The doubt that surrounds them is well shown by the fact that each author in turn has been sceptical as to the accuracy of the diagnosis in

most of the cases of his predecessors. It is highly probable that many of them were cases of rhachitis with splenic tumor and anemia, or of anemia with leucocytosis — the anemia infantum pseudoleukemica of v. Jaksch.[21] In the future no such confusion will be possible, as a differential count of the white corpuscles makes the diagnosis positive.

The cases, with dates and ages, are as follows: Golitzinsky,[22] 1861, two cases, eleven months and two weeks respectively; Mosler,[16] 1864, six months; Seitz,[23] 1866, one year; Stilling,[24] 1880, one year; Fagge,[25] 1881, twenty months; Senator,[11] 1882, twins of eighteen months; Ballowitz,[26] 1884, five months; Litten,[27] 1887, eighteen months; Hochsinger and Schiff,[28] 1887, sixteen months; Sänger,[3] 1888, fetus at thirty-second week; v. Jaksch,[21] 1889, fourteen months; Hayem,[18] 1889, ten months; Mayer,[29] 1890, sixteen months; Chaumier,[30] 1890, sixteen months; Ortner,[12] 1891, eight and a half months; Middleton,[31] 1893, sixteen months; Osler,[9] 1893, eight months; Engel,[32] 1894, thirteen months. It is highly probable, however, that not more than half, perhaps not more than a third, of these were really cases of leukemia.

My own case follows: Joe K., one year old, came to the West End Nursery on April 26, 1894, as an out-patient. His parents were both Russians, and, although very poor, seemed well and strong. As far as they knew, no relatives had had any disease of this nature. No history of syphilis could be obtained. Four other children were alive, well and not rhachitic. Two had died of acute disease in Russia. No very definite history of his illness could be obtained. He was weaned at three months, and had been fed exclusively on condensed milk for the last six months. He had been failing gradually for some months, his belly had

been large for two months, and he had been unable to lie on his left side for a month. Never had nose-bleed or hemorrhages from stomach or bowels. Never had any eruption on body. Vomited occasionally, bowels were somewhat constipated, the dejections being light-colored. No cough or pain.

Physical examination showed a markedly atrophic child, very anemic. The head was large, forehead prominent, and anterior fontanelle widely open. Moderate rosary and enlargement of epiphyses, with slight bow-legs. Marked enlargement of glands in neck, axillæ and groins. Heart and lungs normal. Abdomen was very much enlarged but contained no fluid; superficial veins distended. Liver dulness began at upper border of fifth rib in nipple line, and the lower border could be felt round and smooth about two fingers' breadth below the costal border in the same line. The spleen was very much enlarged, coming from beneath the costal margin just outside the parasternal line, running just outside the umbilicus, then beyond the middle line, filling up almost the whole left iliac region. The notch could be plainly felt. Spleen and abdomen not at all tender. No hemorrhagic spots on skin. The blood examination made at this time is given below.

It was impossible to keep the child under observation, but he was seen again on May 28. He had failed rapidly during the month. His skin was very pale with a decided yellow tinge, the face, body and extremities being thickly covered with purpuric spots, varying in size from that of a pin-head to that of a lead-pencil. These spots had appeared two days before, at which time he developed a cough, and refused to eat. Had had no other hemorrhages, bowels were loose, dejections of normal color, no vomiting. Examination of the chest showed a broncho-pneumonia,

involving the lower two-thirds of the left lung, and a well-marked bronchitis in the right. The heart was normal. Abdomen rather more distended, not tender, no fluid. There was a slight increase in the size of both liver and spleen. He was almost moribund, and probably survived but a few days.

The usual association of leukemia with rickets was present in this case, the leukemia probably having developed subsequent to the rhachitis. The latter was undoubtedly due to improper food and surroundings, and it seems more reasonable, in the present state of our knowledge, to consider the leukemia as arising from the same cause rather than as secondary to the rhachitis.

The blood-count, made on April 26th, showed 2,900,000 red corpuscles and 48,000 white per cubic millimetre, giving a proportion of one to sixty. A differential count of 1,000 white corpuscles on slips, dried and stained with Ehrlich's *triple* stain, resulted as follows:

Small lymphocytes	234 = 23.4 %
Large lymphocytes and transition forms	81 = 8.1 %
Myelocytes	214 = 21.4 %
Polynuclear neutrophiles	465 = 46.5 %
Eosinophiles	6 = .6 %

The classification is that recommended by Thayer.[33] Slips stained with eosin and methylene-blue showed numerous mononuclear and polynuclear cells with fine granulations which took the eosinophile stain feebly. Slips stained with dahlia showed the presence of a very few "mastzellen." Numerous partially destroyed cells, both mononuclear and polynuclear, were met with.

The red corpuscles were also of much interest, many forms being met with. There was a very marked poikilocytosis, a moderate number of microcytes, and

many macrocytes, many of these being three times the diameter of a normal red corpuscle. Many of all these forms lacked the normal concavity. Nucleated red corpuscles were present in great abundance. No microblasts were seen, however. Many cells, the size of normal corpuscles, were met with in which the nucleus was small, feebly stained, and with little nuclear structure, the protoplasm being not quite homogeneous — "wrinkled," as it were — and staining a reddish-violet. These may, perhaps, be regarded as undeveloped normoblasts. Normoblasts were very abundant, always with one nucleus, which showed a well-developed nuclear structure, and which occasionally presented indentations, as if division was beginning. The nucleus was rarely in the centre, often on the side, sometimes half way out of the cell, and occasionally free. The protoplasm was ordinarily narrow, but sometimes wide. A few cells were met with from which the nucleus had probably escaped. Megaloblasts were quite numerous and presented the same variations as the normoblasts. In addition to these, a number of large oval cells were seen, which contained two nuclei, the long diameter of the cell being about four times that of a normal red corpuscle. In several of these well-marked karyokinetic figures were present. These variations in the erythrocytes of course merely show a severe grade of secondary anemia. The presence of myelocytes in conjunction with the general glandular enlargement and the increased relative proportion of lymphocytes plainly places the case among the mixed forms of leukemia.

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